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Hepato-Gastro-Enterology

A Rare Case of Acute Hepatitis Following Therapy with Sulpiride

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Abstract | **Case Report**

Acute hepatitis by the antipsychotic and neuroleptic drug sulpiride is exceptional and literature data on this subject are limited. We report the case of a 24 year old man with no particular pathological history who was admitted for moderate acute drug-induced hepatitis after one month of treatment with sulpiride 100 mg/day for anxiety. A good clinical and biological evolution was noted in our patient after stopping the drug.

Keywords: Acute drug-induced hepatitis, Sulpiride, Drug-induced liver injury (DILI).

INTRODUCTION

Sulpiride is an antipsychotic of the benzamide family classified as an atypical neuroleptic [1]. Pharmacologically, these molecules are characterized by their elective binding to dopaminergic receptors of the D2 and D3 subtypes, which they block, a localization of effects that is more limbic than striatal, and a bipolar action, predominantly on presynaptic auto receptors at a usual dose of 100 to 800 mg/day, and on postsynaptic receptors at a dose of more than 800 mg/day [1, 2]. Indications for treatment with sulpiride are acute psychotic states, chronic psychotic states (schizophrenia, chronic delusions) [3], short-term treatment of vertigo [4] and anxiety in adults [5].

We report an exceptional case of acute hepatitis caused by the use of sulpiride.

CASE REPORT

24 year old man, neither smoker nor alcoholic, with a history of anxiety, treated with sulpiride 100 mg/day. After one month of treatment, the patient developed asthenia associated with generalized mucocutaneous jaundice. On interrogation the patient had no history of liver or biliary pathologies, no other medication taken during the last 3 months, no herbal medicine taken, no blood transfusion and no sexual relations at risk. The patient was hemodynamically and respiratory stable and apyretic.

On clinical examination no abdominal pain, no abdominal masses, no bleeding syndrome or neurological disorder.

The diagnosis of an acute moderate hepatitis retained in front of a hepatic cytolysis superior to ten times the normal with a level of alanine aminotransferase (ALT): 550 UI/L (normal 10-40 UI/L), aspartate aminotransferase (AST): 490 UI/L (normal 08-38 UI/L) and an international normalized ration (INR): 1.2, the rest of the check-up of repercussion is made (table 1).

Table 1: Blood work-up of acute hepatitis

Lab	Value	Range
ALT	550 IU/l	10-40 IU/l
AST	490 IU/l	08-38 IU/l
alkaline phosphatase	158 IU/l	40-138 IU/l
gamma-glutamyl transferase	65 U/l	10-45 U/l
Total bilirubin	42 gmol /l	< 17 gmol /l
Conjugated bilirubin	35 gmol /l	< 05 gmol /l

Lab	Value	Range
INR	1.2	1
Albumin	42	35-45 g/l
Creatine kinase	10 IU/l	< 190 IU/l
Hemoglobin	14 g/dl	13-17 g/dl
Leukocytes	5.5 G/l	4-10 G/l
mean corpuscular volume	85 fL	80-100 fl
Urea	0.31 g/l	0.15-0.45 g/l
Creatinin	80 pmol /l	65-120 pmol /l
C-reactive protein	4 mg/l	< 05 mg/l
Glycemia	1.07	0.7-0.1 g/l

An etiological workup was performed which was negative for viral serologies: Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), Hepatitis E virus (HEV), Cetomegalovirus (CMV), Epstein Bar virus (EBV), Herpes simplex virus (HSV), Human immunodeficiency virus (HIV), and research for autoimmune diseases, Wilson's disease, and hemochromatosis was also negative. A liver ultrasound showing a thin-walled alithiasic gallbladder with no intrahepatic or extrahepatic bile duct dilatation and no hepatomegaly (Figure 1).

The liver biopsy shows a moderate infiltration by eosinophilic cells and lymphocytes (Figure 2).

Table 2: Etiological work-up for acute hepatitis

Disease	Testing	Results
Hepatitis A virus (HAV)	Anti-HAV IgM	Negative
Hepatitis B virus (HBV)	HBsAg, IgM anti-HBc, HBV DNA	Negative
Hepatitis C virus (HCV)	anti-HCV, HCV RNA	Negative
Hepatitis E virus (HEV)	IgM anti-HEV, HEV RNA	Negative
Cetomegalovirus (CMV)	IgM anti-CMV, IgG anti-CMV	Negative
Epstein Bar virus (EBV)	IgM anti-EBV, IgG anti-EBV	Negative
Herpes simplex virus (HSV)	IgM anti-HSV	Negative
Wilson	Ceruloplasmin	Normal
Hemochromatosis	Ferretin, transferrin saturation	Normal
Autoimmune hepatitis	-anti nucleaires antibodies, anti-smooth muscle antibody, anti-LKM1 antibodies & anti-mitochondrial antibodies titres	-Negative
	- serum immunoglobulin IgG,IgA,IgM	-normal

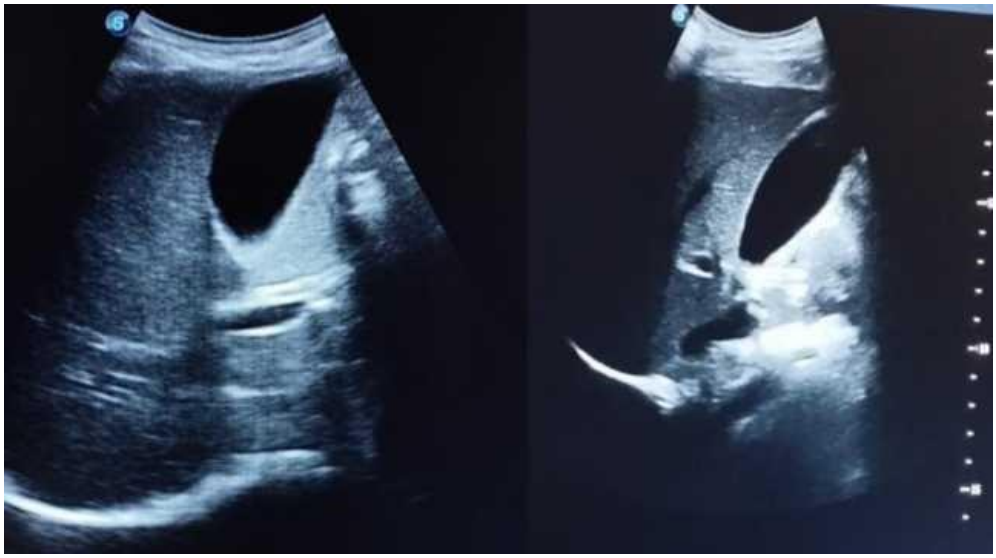

Figure 1: Hepatic ultrasound: alithiasic gallbladder and the main bile duct fine

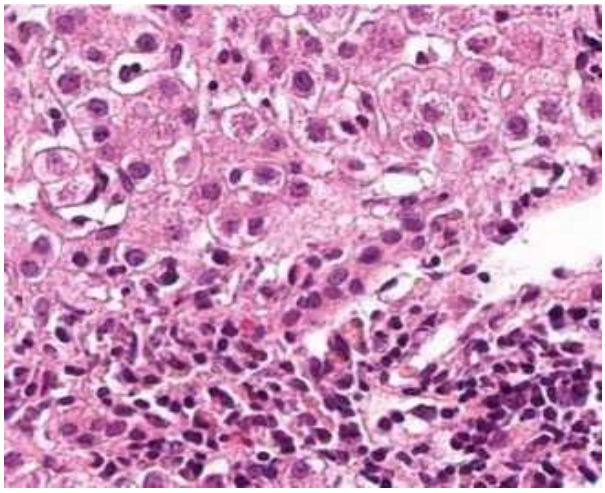

Figure 2: Liver biopsy showing a lymphocytes infiltrate

The patient has a moderate acute hepatitis with no serious signs, no neurological disorder, no disorder of consciousness, no organ dysfunction or serious coagulation disorder not requiring hospitalization.

The management is to stop taking Sulpiride and stop all hepatotoxic drugs, clinical and biological monitoring every week and contact the pharmacovigilance center.

The evolution marked by a disappearance of jaundice after 3 weeks with a normalization of the liver markers (AST, ALT, Total bilirubin) one month after stopping Sulpiride.

DISCUSSION

Drug-induced liver injury (DILI) is one of the most challenging liver disorders faced by hepatologists, because of the myriad of drugs used in clinical practice, the ability of the condition to present with a variety of clinical and pathological phenotypes and the current absence of specific biomarkers [6]. It is mostly a diagnosis of exclusion that relies on multiple elements in the medical history, presentation, laboratory data, and subsequent disease course [7]. The principal parameters are: the time to onset, clinical features, including the type of liver injury, cholestatic, hepatocellular, or mixed pattern, the time and course of recovery, specific risk factors, and the exclusion of other diagnoses and previous reports of the hepatotoxicity of the incriminated agent [8].

Les medicaments may cause a wide spectrum of liver injury, affecting all cells present in the liver and biliary tree, and ranging from mild asymptomatic liver enzyme elevation to acute hepatitis, chronic hepatitis, cirrhosis, liver failure, acute and chronic cholangitis, macro- and microvesicular steatosis, and vascular lesions [9].

Cytochrome P450 (in the liver) is responsible for the metabolization of most antipsychotics [10],but sulpiride remains the least hepatotoxic and the neurolyptic of choice in case of disturbed liver function [11] because the elimination of sulpride is primarily through the kidney and hepatic metabolism is of minor significance and results in formation of primarily inactive metabolites [12, 13].

Very rare cases of acute hepatitis followed by recovery have been reported [14-16] (Table 3).

However, when sulpiride is suspected to be the etiology of acute hepatitis, then it should be interrupted and an alternative treatment should be considered [11].

Table 3: Literature reports of liver injury secondary to sulpiride

Author	Age	Type of lesion hepatic	Dose	Treatment time
Melzer E & Knobel B. 1987 [16]	51	Acute cholystatic hepatitis	150 mg/day	3 weeks
Villari D & Rubino F 1995 [15]	59	Ductopenia	100 mg/day	11 months
Ohmoto K & Yamamoto S 1999 [14]	66	Primary biliary cholangia	Not specified	3 months
Our case (2022)	24	Acute cytolytic hepatitis	100 mg/day	4 weeks

CONCLUSION

Acute hepatitis caused by sulpiride drug is an exceptional entity because it is the least hepatotoxic of the neuroleptic drugs and the treatment of choice in case of liver balance disturbance.

Since the diagnosis is sometimes difficult, an exhaustive assessment is required before selecting the drug in question.

Acute hepatitis with sulpiride is usually mild and resolves after discontinuation of the drug.

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